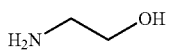
COMPOSITIONS AND METHODS FOR STABILIZING SUSCEPTIBLE COMPOUNDS

[0001] This application claims the benefit of U.S. Provisional Application No. 61/440,237, filed Feb. 7, 2011, under 35 U.S.C. § 119(e), whose disclosure is incorporated by reference in its entirety.

[0002] Some chemicals are known to degrade over time, even when they are in dry formulations, either in the presence of moisture, or due to gradual interaction with other components within the formulation. This is commonly seen in the pharmaceutical industry, food industry, and even in the cell culture media industry and it contributes to shorter shelf-life of the product. For instance, ethanolamine, is a susceptible compound in cell culture media and degrades over time, contributing to shorter shelf-life of the cell culture media. Ethanolamine, also known as 2-amino ethanol or monoethanolamine, is an alkanolamine characterized by the presence of both an amine group and a hydroxyl group and has the following chemical structure:



[0003] Ethanolamine is commonly used in the chemical industry as a component in detergents, pharmaceuticals, and cosmetics. For example, it is used in both water-based and solvent-based coatings to enhance the solubility, reducibility, pigment dispersing, and pH stability. Ethanolamine is also used in the water treatment industry, and more particularly in the steam cycles of power plants, to prevent corrosion of metal components. It is also used to scrub or remove acidic components, such as hydrogen sulfide and carbon dioxide from gas streams in natural and refinery gas operations. Ethanolamine is produced by the reaction of ethylene oxide with ammonia, along with the additional secondary products of diethanolamine and triethanolamine.

[0004] Cell culture media provide the nutrients necessary to maintain and grow cells in a controlled, artificial and in vitro environment. Media formulations have been used to cultivate a number of cell types including bacterial cells, and eukaryotic cells such as animal, plants, etc. Ethanolamine is a useful component of eukaryotic cell culture media and is generally supplemented later as it is a susceptible component. Ethanolamine can be problematic in certain compositions because of its low stability. For example, in cell culture media, in the presence of amino acids, ethanolamine degrades rapidly. This instability increases in a warmer environments, such as that encountered during the process of preparing dry powder cell culture media, resulting in ethanolamine degradation and reduced shelf life of the cell culture media. Similarly, a number of cell culture components such as vitamins, growth factors like insulin, and cytokines, etc., may also be unstable in media formulations, especially in single component dry-format media formulations, which may contain from 60-100 different chemicals of varied reactivities, including amino acids.

[0005] There exists a need for stabilizing and/or protecting labile components present in cell culture media formulations, especially in single component cell culture media formulations, in dry-format media formulations, etc.

SUMMARY

[0006] The present disclosure provides methods for increasing or protecting the stability of a labile compound or component, a sensitive or susceptible component or compound, (terms which may be used interchangeably), in a composition, including but not limited to, a cell culture medium, a cell culture supplement, pharmaceuticals, nutraceuticals, food supplements, vitamin enriched formulations, cosmetics, detergents, etc.

[0007] Thus, in one embodiment, the disclosure is directed to composition, like a cell culture composition, comprising a protected labile molecule, wherein the protected labile molecule is prevented from adverse reactions with a cell culture component in the cell culture composition. In certain embodiments, the cell culture composition may be a dry-format cell culture powder whereas in other, it may be a liquid cell culture medium. In a further embodiment, the protected labile molecule may be selected from any labile molecule in a group consisting of molecules like ethanolamine, a growth factor, a vitamin, a cytokine, etc. In some embodiments, the labile molecule may be protected by derivatization of the labile molecule or by sequestration of the labile molecule. In one aspect of this embodiment, the labile molecule is ethanolamine. In another aspect of this embodiment, the protected labile molecule may be a growth factor like insulin, or a vitamin like B12, or thiamine, etc.

[0008] By a 'labile molecule, component or compound', or 'a susceptible molecule, component or compound' is meant, one that is prone to degradation or an unwanted interaction with other components in the same composition, for e.g., polyamines like ethanolamine, vitamins, growth factors, etc. in compositions such as culture media, supplements, pharmaceuticals, nutraceuticals, food supplements, vitamin enriched formulations, cosmetics, detergents, etc., where these components degrade quickly or over periods of time during storage due to unwanted interactions with other chemicals within the same composition.

[0009] In a further aspect of the above embodiment, the cell culture composition comprises a protected labile molecule wherein the protected labile molecule demonstrates enhanced stability in the cell culture composition, and wherein the labile molecule is ethanolamine. In a further embodiment, the cell culture composition may be a dry-format cell culture powder or a liquid cell culture medium.

[0010] In a preferred embodiment, the ethanolamine is protected by either derivatization or by sequestration. The derivatization may be by reaction with a sugar alcohol, or an amino sugar, or an uronic acid, or a phosphorylated sugar.

[0011] In a further embodiment, the sugar alcohol may be selected from the group consisting of allitol, altritol, fructitol, galactitol, glucitol, gulitol, iditol, mannitol, sorbitol, talitol, tagatitol, arabinitol, ribitol, ribulitol, xylitol, xylulitol, lyxitol, erythrulitol, erythritol, and threitol.

[0012] In yet another embodiment, the amino sugar may be selected from the group consisting of allosamine, altrosamine, fructosamine, galactosamine, glucosamine, gulosamine, idosamine, mannosamine, sorbosamine, talosamine, tagatosamine, arabinosamine, ribosamine, ribulosamine, xylosamine, xylulosamine, lyxosamine, erythrulosamine, erythrosamine, and threosamine.

[0013] In another embodiment, the uronic acid may be selected from the group consisting of alluronic acid, altruronic acid, fructuronic acid, galacturonic acid, glucuronic acid, guluronic acid, iduronic acid, mannuronic acid, sorbu-